REMARKS

I. Specification Amendments

The specification has been objected to because the abstract must be a single paragraph.

As noted above, a replacement abstract has been submitted herewith. Accordingly, Applicants respectfully request reconsideration and withdrawal of this objection.

II. Claim Amendments

By the foregoing amendments to the claims, claim 1 has been amended by deleting the phrase "corresponding to said anticoagulated plasma" from step (a). Furthermore, claim 10 has been amended to correct "activated partial prothrombin time (APTT)" to "activated partial thromboplastin time (APTT)."

The amendments to the claims have been made without prejudice or disclaimer to any subject matter recited or canceled herein. Applicants reserve the right to file one or more continuation and/or divisional applications directed to any canceled subject matter. No new matter has been added, and entry of the foregoing amendments to the claims is respectfully requested.

III. Response to Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-15 have been rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for a number of reasons.

This rejection is respectfully traversed.

As described throughout the application (see, e.g., page 13, lines 18-29, of the specification as filed) the present invention relates to methods for determining an analyte concentration in anticoagulated plasma by performing two or more different measurements on a mixture of the corresponding blood and liquid reagent. At least one of the measurements must correlate to the hematocrit of the blood and at least one of the measurements must correlate to the analyte concentration of the blood. The analyte concentration for anticoagulated plasma, generally a more clinically useful value than analyte concentration for whole blood, is then determined by computation. The computation is described at least at pages 18-22 of the

specification as filed. With regard to analytes, the application describes, for example, the PT analyte (see page 17, line 35, to page 18, line 3).

It is respectfully submitted that the present claims particularly point out and distinctly claim the subject matter Applicants regard as the invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

IV. Response to Claim Rejections Under 35 U.S.C. §§ 102 and 103

A. Claims 1, 2, 7-10, 12, and 15 have been rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Owren (1959).

B. Claims 1-4, 7-9, 12, and 15 have been rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Beresini (1993).

C. Claims 1 and 11 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over the combination of Beresini and Zhang (2000).

D. Claims 1, 13, and 14 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over the combination of Beresini and Potzsch (1997).

These rejections are respectfully traversed.

The field of the invention is point of care wet-chemistry analysis where a blood sample is analyzed for its content, or level, of an analyte of interest. The aim of the analysis is to express the analytical results in such a way that it as closely as possible equals the content, or level, of the analyte had an anticoagulated blood sample or coagulated sample been sent to a hospital laboratory where the content, or level, of the analyte had been determined in plasma or serum also by wet-chemistry analysis. It is of interest to do the point of care analysis also in milieus where good precision in allotment of the volumes of sample and reagent that are mixed cannot always be achieved.

The invention provides an inventive way of doing this in which the pivotal step is to perform at least two different determinations on a mixture of sample and reagent, at least one of the determinations is such that its result is dependent on, i.e. correlates to, the hematocrit of the sample, at least one of the determinations is such that its result is dependent on, i.e. correlates to, the analyte content, or level, of the sample. This allows, by computation, under the assumption that the allotment of volumes is sufficiently correct, the analyte content, or level, to be expressed

in such a way that it more closely harmonizes to the analyte content, or level, obtained by the hospital laboratory. This also allows, by computation, if the hematocrit is known by separate determination, to first correct for the incorrectness of the allotments of the volumes, and to expressed the results of the point of care determination in such a way that it more closely harmonizes to the analyte content, or level, obtained by the hospital laboratory.

In Owren 1959 there is no mention of performing two determinations on a mixture of sample and reagent of which one is dependent on the hematocrit. Therefore there is nothing in this document that anticipates the invention. And, in all the years since 1959, there is no description of a thrombotest, or prothrombin time test, that is performed in such a way that at least two determinations are performed on the mixture of sample and reagent of which at least one is dependent on hematocrit. And this is in spite of the advantages such a procedure offers, and this in spite of the fact that some one billion such test are performed each year.

The fact that the hematocrit of the sample affects the outcome of several kinds of wet-chemistry analyte determinations performed on blood samples is common knowledge. What is meant by affecting is, that the agreement between the blood analysis and a hospital determination on the same sample will agree less well if the hematocrit is "extreme", i.e. far from normal. The invention provides a novel, practical way to deal with the fact.

It is also appreciated, at least since1959, that if the hematocrit is known (by a separate determination), then something can be done to make the results of the blood analysis agree better with the hospital ditto, as described by Owren, but it is then always done under the assumption that the allotment of volumes is sufficiently correct. In this case, the case where the hematocrit is known by separate determination, the invention provides more than Owren mentions, it provides also a possibility to correct for incorrect allotments of volumes.

Zang et al 2000 describes that a separate determination of hematocrit can be performed in an noninvasive way. It may be the case that by practicing the method described by Zang et al the hematocrit of the blood can become known. However, Zang et al does not teach or even suggest the subject matter of the present claims.

Beresini et al 1993 describe a procedure, an assay, to determine cyclosporine in whole blood. Already in the abstract it is declared that the "neither extreme values of hematocrit nor choice of anticoagulant affected cyclosporine (CsA) recovery". The assay described by Beresini

was thus not affected by hematocrit and cannot be improved by practicing the invention particularly in cases where the hematocrit was unknown by separate determination. If the hematocrit was known the practice of the invention could still be of value since it could be used to correct for effects of incorrect allotment of sample and reagent volumes. In no particular way, less than many other wet-chemistry analytical procedure, actually, since the assay is not affected by hematocrit, does the work of Beresini et al anticipate the invention. Combining the results and conclusions of Beresini et al with those of Zang et al 2000 does not bring a person skilled in the arts any closer to the present invention. In fact, thorough study of Beresini et al would distant a person skilled in the art from anticipating the invention because the person may come to think, that all, or at least many, assays could be modified to resemble the one described by Beresini, and could also be made insensitive to extreme values of hematocrit, like the one of Beresini, and thus circumventing the problem of the influence/dependence of extreme hematocrit on quantitative, wet-chemistry analysis of blood.

Pötzsch et al 1997 establish a plasma based ecarin clotting time assay that is superior to APTT, an assay only limitedly inferior to the more tedious chomogenic assays, in determining the level of hirudin in anticoagulated plasma. Pötzsch et al mention nothing on analysis of blood. The scope of Pötzsch et al is strictly limited to analysis of anticoagulated plasma, and because of this, there is no way that combining Pötzsch et al with Bersini 1993, or with Zang 2000, or with anything, that will aid in reaching the invention of claim 1.

Pötzsch et al do mention that the ecarin clotting time assay studied is affected by fibrinogen, and establish a limit for satisfactory function of their assay to above 0,5 g/l (50 mg/dl) of fibrinogen in the plasma sample, see FIG. 1B on page 377. There is no mention of adding fibrinogen to the reagent as in claim 13, a claim dependent on claim 1.

Pötzsch el al mention prothrombin time as they explore the use of their assay on plasmas from patients on oral anticoagulation, plasmas with INR in the range from 0,93 to 6,0, see FIG. 4B on page 380. There is no mention of the possibilities of re-expressing INR into PT% as in claim 14, a claim dependent on claim 1.

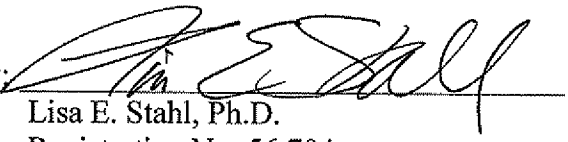
In view of the above, Applicants respectfully request reconsideration and withdrawal of these rejections.

CONCLUSION

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions related to this response, or the application in general, it would be appreciated if the Examiner would telephone the undersigned attorney at the below-listed telephone number concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

By: 
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